

Amivantamab Plus Lazertinib vs Osimertinib in First-line *EGFR*- mutant Advanced NSCLC *Final Overall Survival from MARIPOSA*

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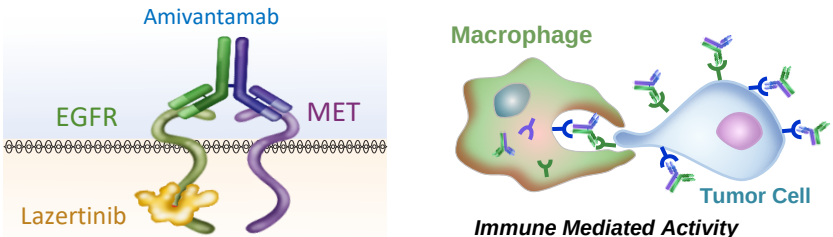
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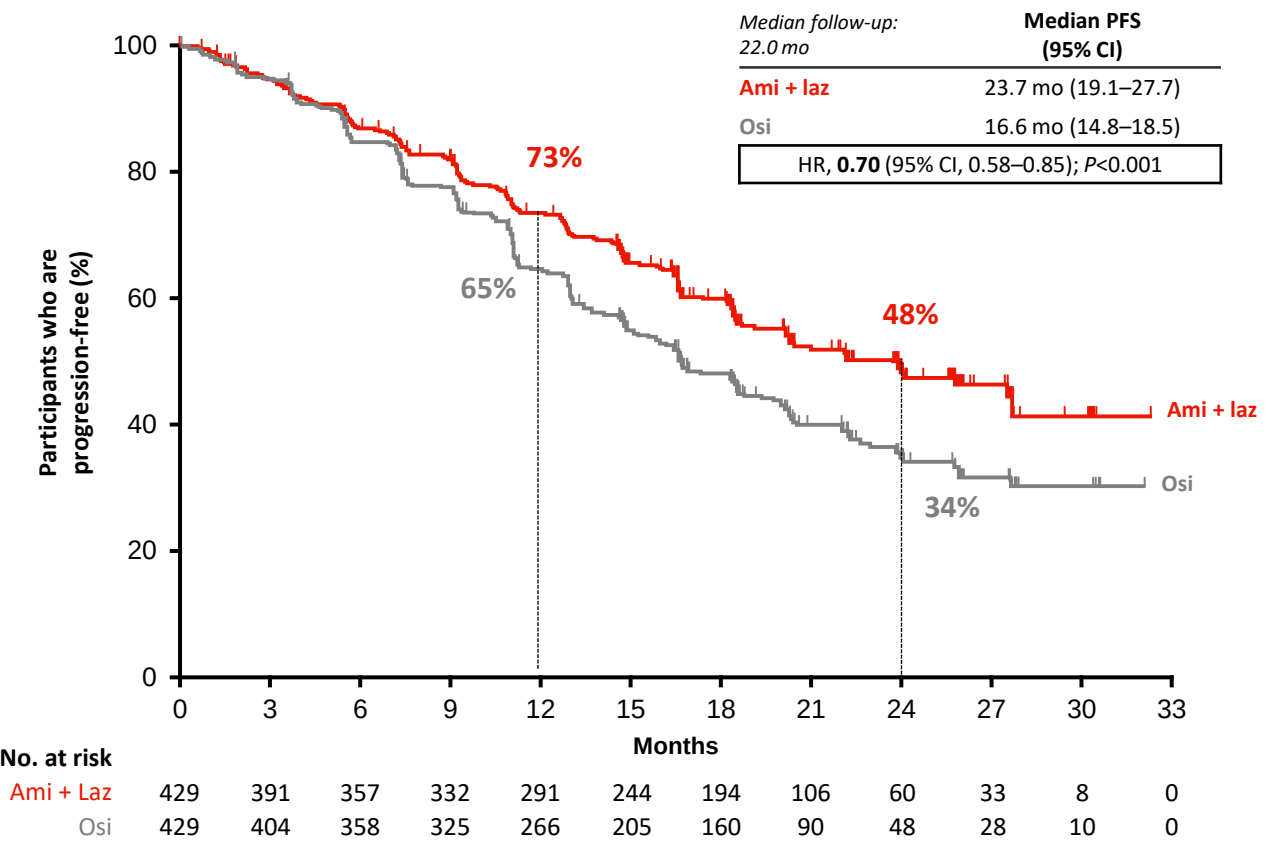
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Background

- In MARIPOSA, 1L amivantamab + lazertinib significantly improved PFS vs osimertinib^{1,2}
- Amivantamab + lazertinib is approved for patients with 1L *EGFR*-mutant advanced NSCLC^{3,4}
- 1L amivantamab + lazertinib exhibits a triple mechanism of action with a reduction in the spectrum and complexity of acquired resistance⁵



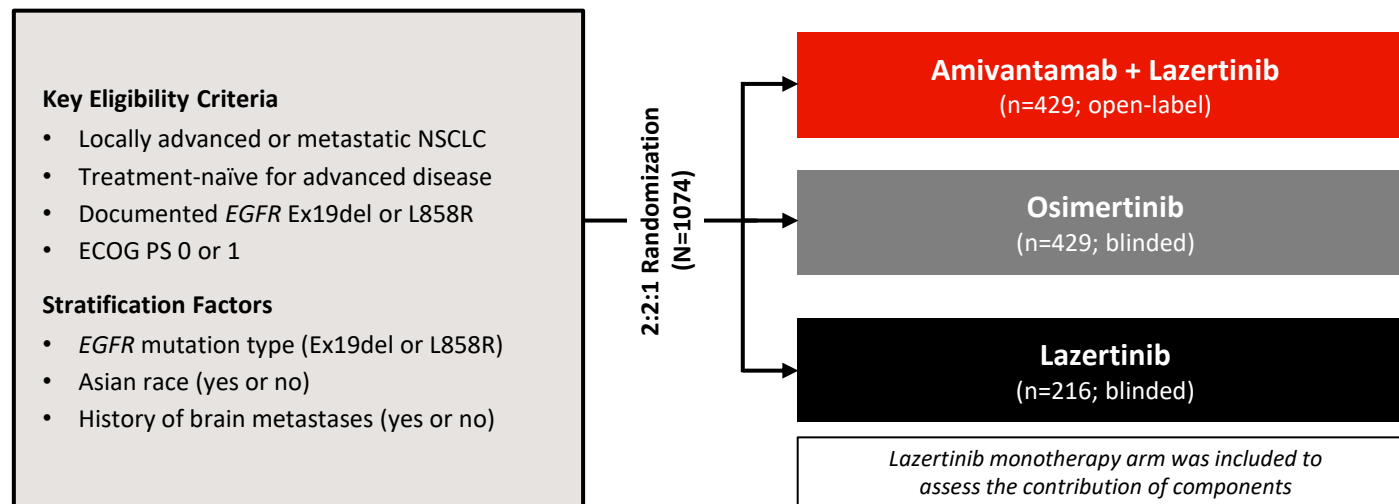
1L Amivantamab + Lazertinib
Primary Endpoint: PFS by BICR^{1,2}



Here, we report the protocol-specified final overall survival results of 1L amivantamab + lazertinib vs osimertinib from MARIPOSA

1. Cho BC, et al. *N Engl J Med.* 2024;391(16):1489-1498. 2. Cho BC, et al. Presented at the European Society for Medical Oncology (ESMO) Congress; October 20-24, 2023; Madrid, Spain. 3. RYBREVANT® (amivantamab-vmjw) injection for intravenous use [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2025. 4. Johnson & Johnson. European Commission approves LAZCLUZE® (lazertinib) in combination with RYBREVANT® (amivantamab) for the first-line treatment of patients with EGFR-mutated advanced non-small cell lung cancer. January 21, 2025. Accessed January 27, 2025. 5. Besse B, et al. Presented at the European Society for Medical Oncology (ESMO) Congress; September 13-17, 2024; Barcelona, Spain.

Phase 3 MARIPOSA study design



Primary endpoint:

- PFS by BICR per RECIST v1.1

Key secondary endpoint:

- Protocol-specified final overall survival

Other endpoints reported in this presentation:

- Intracranial PFS (icPFS)
- Intracranial ORR (icORR)
- Intracranial DoR (icDoR)
- Time to symptomatic progression (TTSP)
- Safety

*Serial brain MRIs were required for all participants
MARIPOSA did not allow treatment-crossover^a*

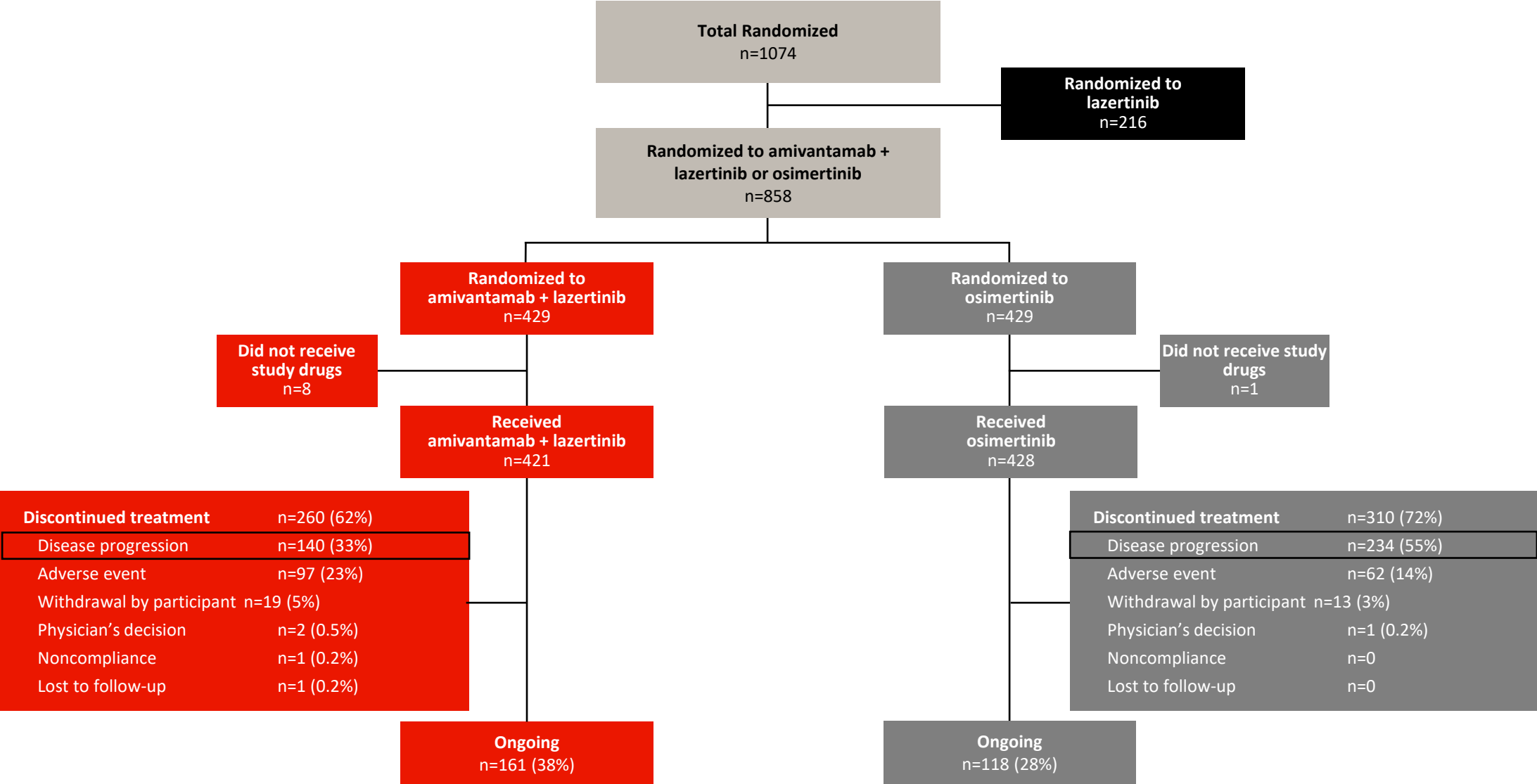
OS was a key secondary endpoint with prespecified alpha to assess significance

- Protocol-specified final OS analysis was planned for when ~390 deaths had occurred in the amivantamab + lazertinib and osimertinib arms
- OS was tested with a 2-sided alpha of 0.05, determined by O'Brien-Fleming alpha spending approach as implemented by the Lan-DeMets method
 - In the prespecified interim analysis, a 2-sided alpha of 0.005 was allocated for OS
- The protocol-specified final analysis of overall survival was subsequently evaluated at a 2-sided significance level of 0.0484

MARIPOSA (ClinicalTrials.gov Identifier: NCT04487080) enrollment period: November 2020 to May 2022; clinical cut-off: 04-Dec-2024. OS analysis was evaluated by means of the P value generated from the stratified log-rank test, with *EGFR* mutation type, Asian race, and history of brain metastases as stratification factors. HRs and 95% CIs were calculated using the stratified Cox regression model with treatment as the sole explanatory variable. Dosing (in 28-day cycles): amivantamab: 1050 mg (1400 mg if ≥80 kg) weekly for the first 4 weeks, then every 2 weeks; lazertinib: 240 mg daily; osimertinib: 80 mg daily.

^aMARIPOSA did not allow crossover as neither amivantamab + lazertinib nor amivantamab + chemotherapy were approved during MARIPOSA enrollment.

Participant disposition



Baseline demographics and clinical characteristics^{1,2}

Baseline characteristics were well balanced across both arms

Characteristic, n (%)	Amivantamab + lazertinib (n=429)	Osimertinib (n=429)
Median age, years (range)	64 (25–88)	63 (28–88)
Female	275 (64)	251 (59)
Race		
Asian	250 (58)	251 (59)
White	164 (38)	165 (38)
Other ^a	15 (3)	13 (3)
ECOG PS 1	288 (67)	280 (65)
History of smoking	130 (30)	134 (31)
History of brain metastases	178 (41)	172 (40)
EGFR mutation type ^b		
Ex19del	258 (60)	257 (60)
L858R	172 (40)	172 (40)
Adenocarcinoma subtype	417 (97)	415 (97)

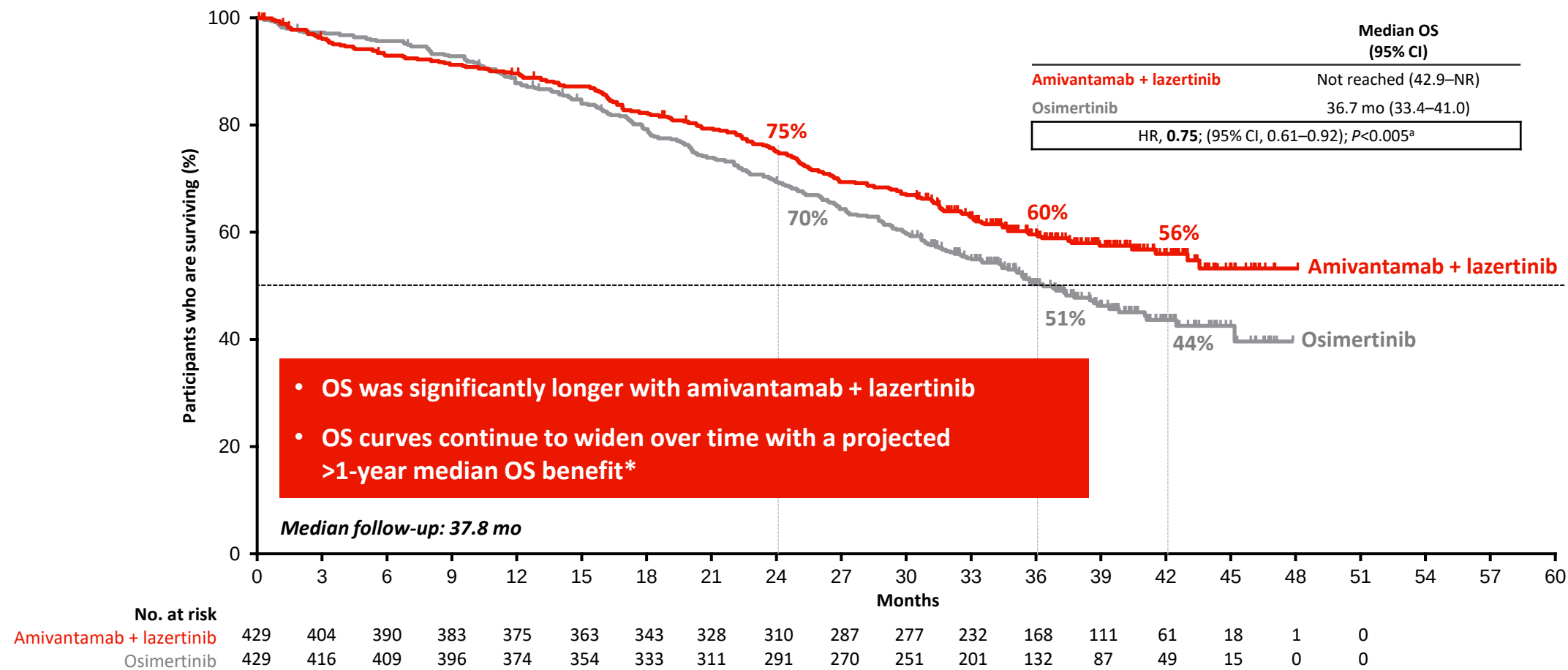
Note: percentages may not sum to 100 due to rounding.

^aOther includes American Indian or Alaska Native, Black or African-American, multiple, and unknown.

^bOne patient in the amivantamab + lazertinib arm had both Ex19del and L858R.

1. Cho BC, et al. *N Engl J Med*. 2024; 24;391(16):1486-1498. 2. Cho BC, et al. Presented at the European Society for Medical Oncology (ESMO) Congress; October 20-24, 2023; Madrid, Spain.

MARIPOSA: overall survival

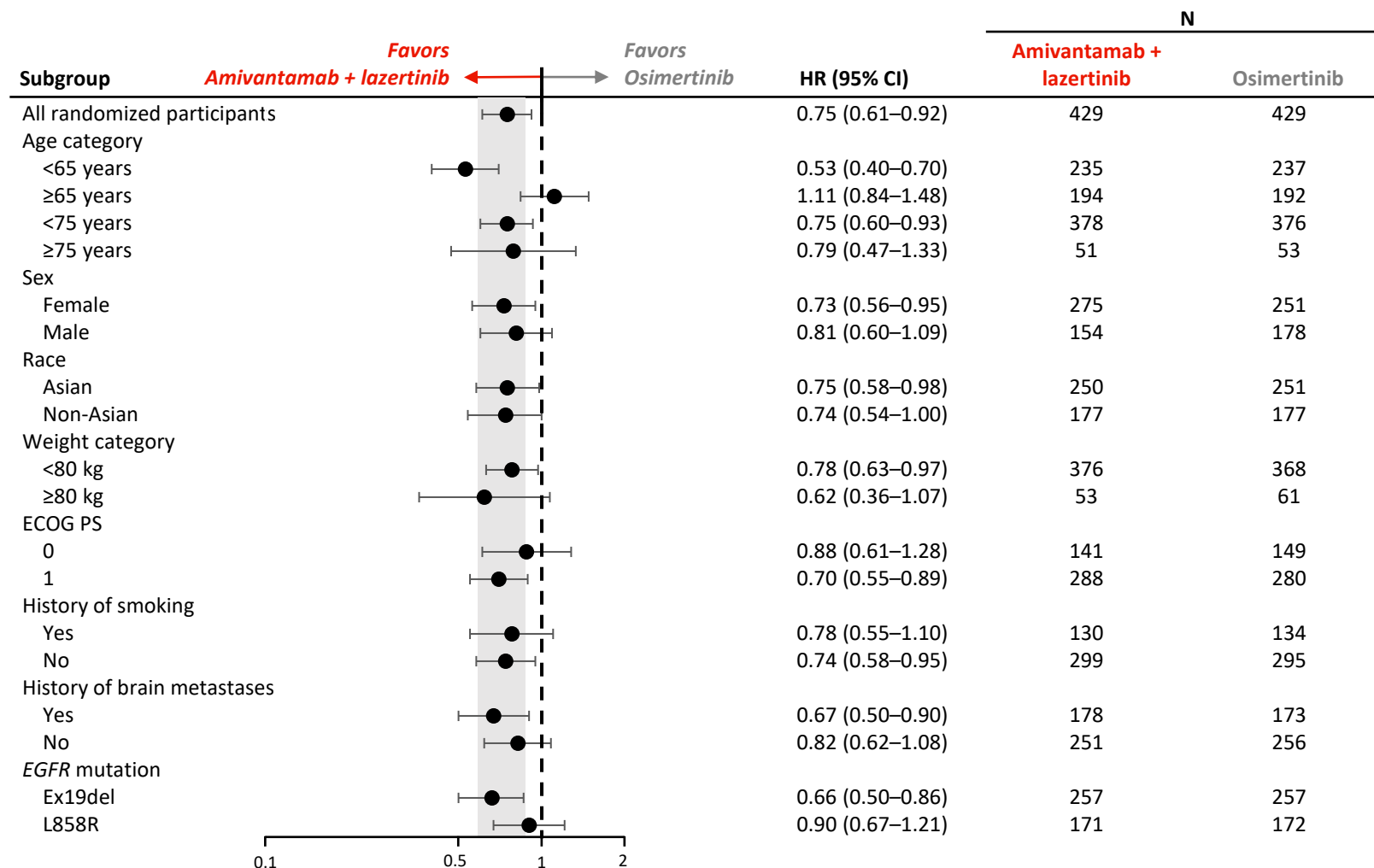


*Based on the observed hazard ratio and median overall survival in the osimertinib group, with an exponential distribution assumption of overall survival in both groups, amivantamab-lazertinib is projected to provide an overall median survival benefit exceeding 12 months compared with osimertinib.

Note: Last participant was enrolled in May 2022. Clinical cutoff date was December 4, 2024.
^aP-value was calculated from a log-rank test stratified by mutation type (Ex19del or L858R), race (Asian or Non-Asian), and history of brain metastasis (present or absent). Hazard ratio was calculated from a stratified Cox regression model.

Overall survival in predefined subgroups^a

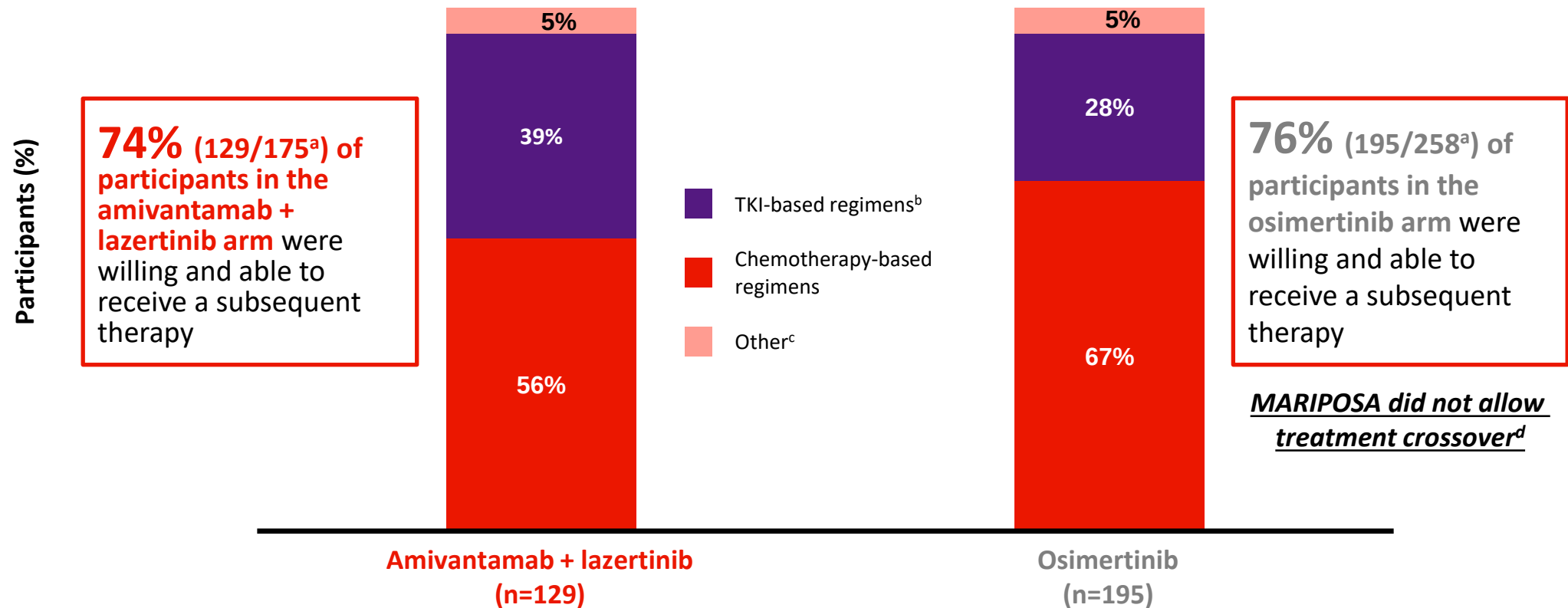
A generally consistent OS benefit for amivantamab + lazertinib over osimertinib was observed across predefined subgroups



Note: Gray box indicates 95% CI of HR for all randomized participants. ^aSubgroup analyses were not part of the hypothesis testing of the trial and should not be used to infer definitive treatment effects.

First subsequent therapy

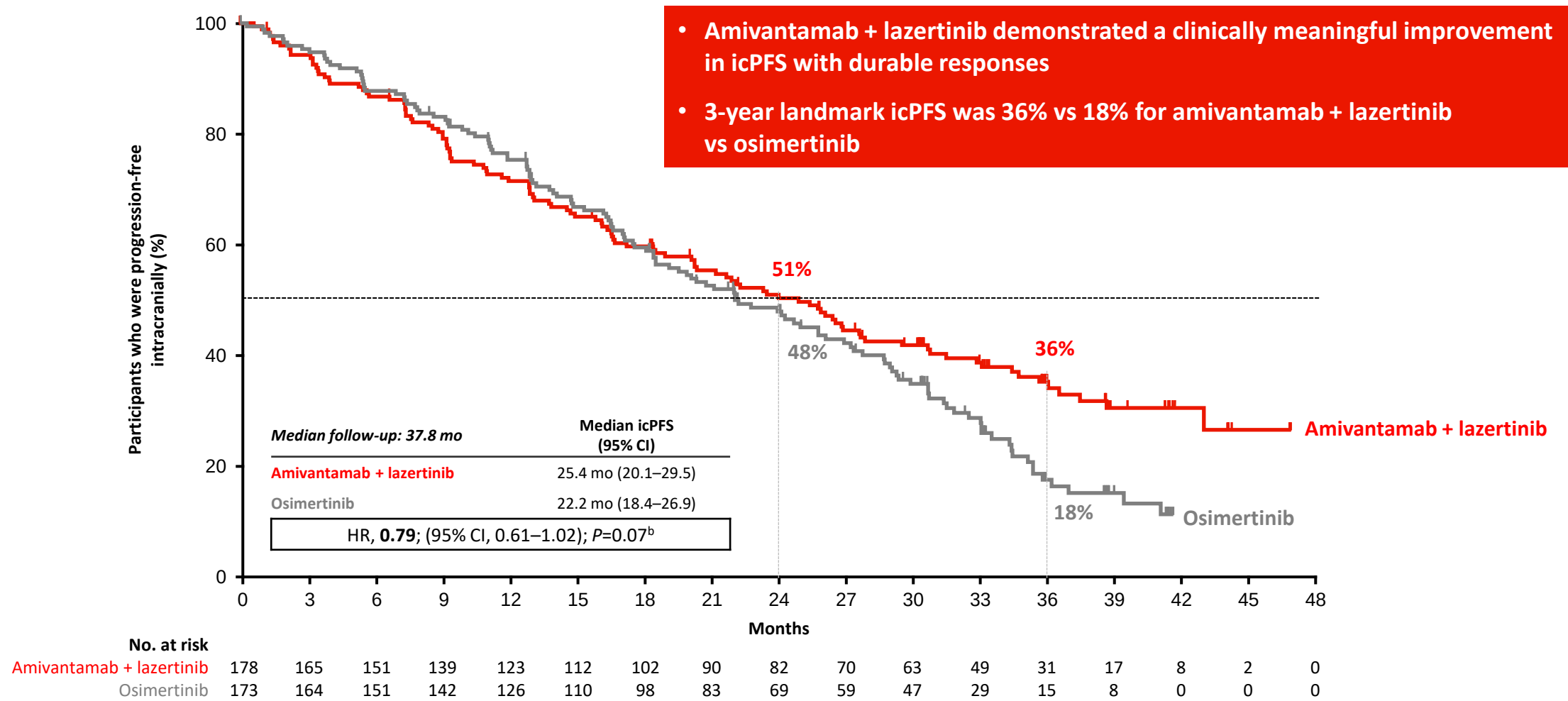
Most common subsequent therapy class was chemotherapy-based regimens in both arms



74% received 2L therapy, suggesting a long-term treatment plan after 1L amivantamab + lazertinib is feasible

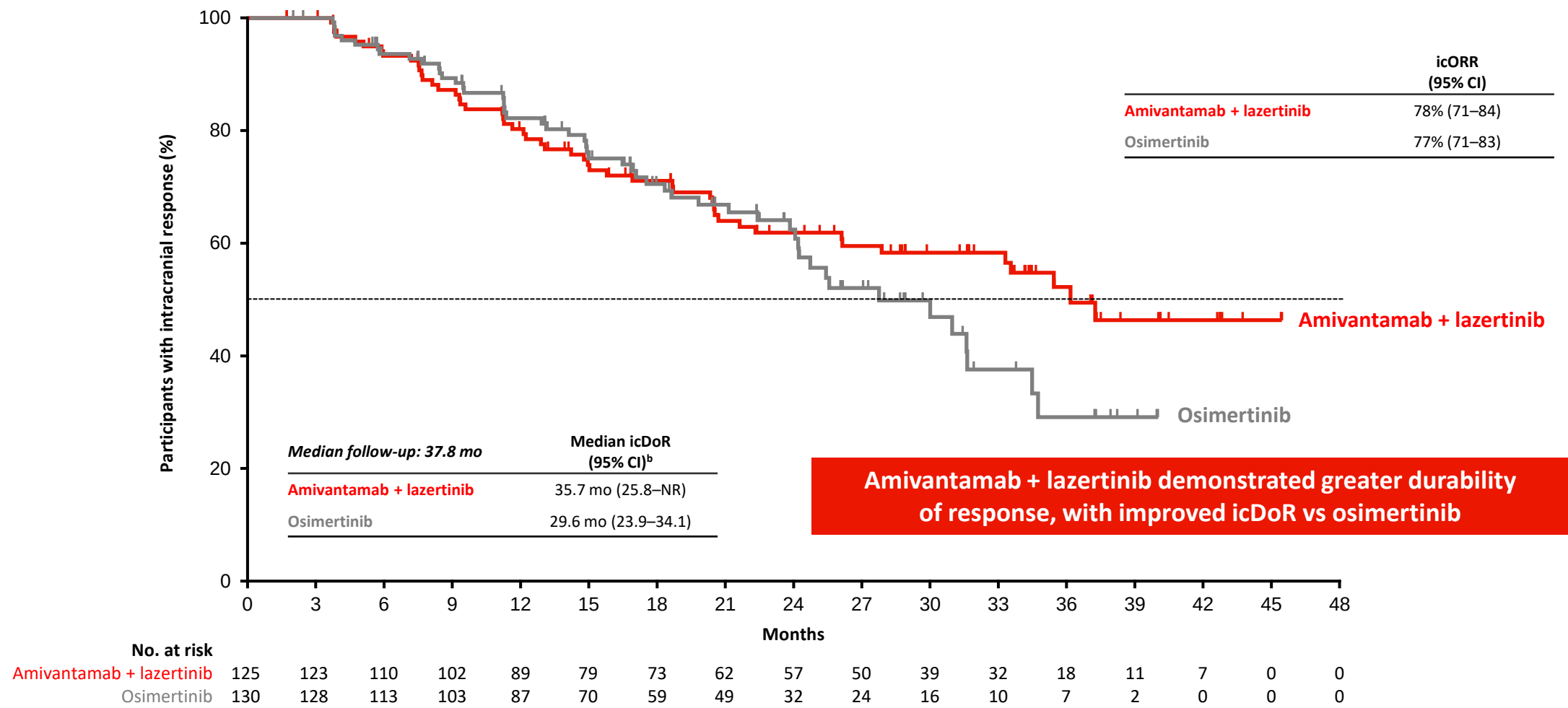
Note: Percentages may not total 100 due to rounding. ^aDenominator is the number of participants who had disease progression and discontinued randomized treatment. ^bTKI-based regimens include TKI + chemotherapy (5% in both arms). ^cOther therapy included VEGFi alone, IO alone, herbals, antibody-drug conjugates, ALK tyrosine kinase inhibitors, c-MET tyrosine kinase inhibitors, amivantamab (1 participant received amivantamab-chemotherapy after amivantamab-lazertinib; after osimertinib, 1 participant received amivantamab-chemotherapy, 1 participant received amivantamab-lazertinib, and 1 participant received amivantamab monotherapy), and investigational agents. ^dMARIPOSA did not allow crossover as amivantamab-based regimens were not approved in the 2L setting during MARIPOSA enrollment.

Intracranial PFS^a



^aIntracranial PFS was defined as time from randomization until the date of intracranial disease progression (progression of brain metastasis or occurrence of new brain lesions) or death, based on BICR using RECIST v1.1 among participants with a history of brain metastases. ^b P -value was calculated from a log-rank test stratified by mutation type (Ex19del or L858R) and race (Asian or Non-Asian). Hazard ratio was calculated from a stratified Cox regression model.

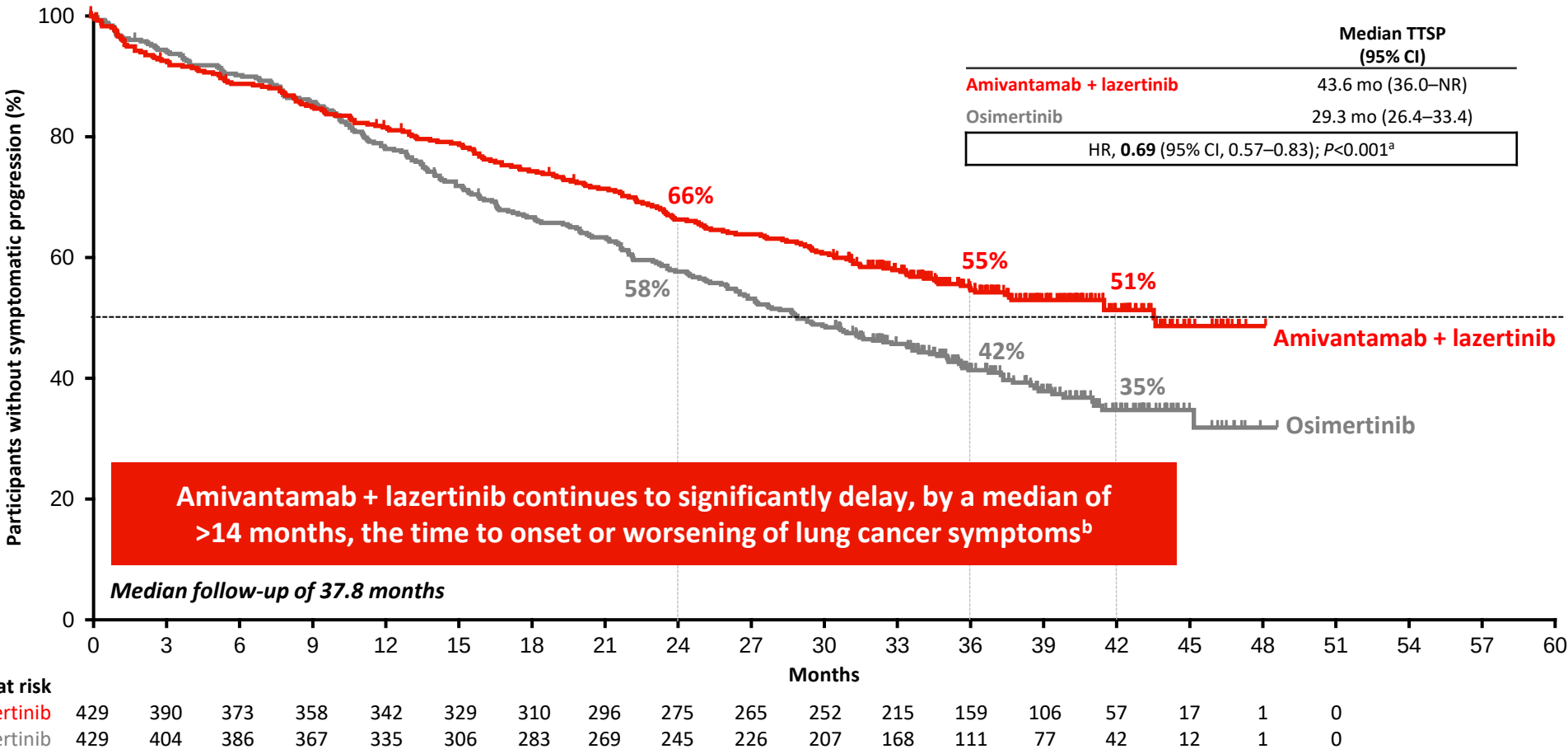
Intracranial DoR^a



^aIntracranial DoR was defined as the time from the date of first documented intracranial response (CR or PR) until the date of documented intracranial progression or death, whichever occurred first, among participants with a history of brain metastases at screening who have intracranial CR or PR based on BICR using RECIST v1.1. ^b95% CIs were estimated with the Kaplan-Meier method.

Time to Symptomatic Progression (TTSP)

Symptomatic progression is a patient-relevant endpoint that measures time from randomization to the onset of new/worsening lung cancer symptoms requiring a change in therapy, clinical intervention, or death, based on investigator discretion



^a P -value is calculated by log-rank test stratified by mutation type (Ex19del or L858R), race (Asian or Non-Asian), and history of brain metastasis (present or absent). Hazard ratio was calculated from a stratified Cox regression model. ^bData with median follow-up of 22.0 months were previously presented: Nguyen D, et al. Presented at the World Conference on Lung Cancer (WCLC) Congress; September 7-10, 2024; San Diego, CA, USA.

Safety

- Median duration of treatment was **27.0 mo** for amivantamab + lazertinib and **22.4 mo** for osimertinib
- Safety profile was consistent with the primary analysis¹
 - AEs were mostly EGFR- and MET-related and grades 1–2^{1,2}
- A minority of participants were prescribed antibiotics for rash (21%) at study initiation²
- Few were on anticoagulation (5%) at baseline,² with VTE^a occurring in **40%** in the amivantamab + lazertinib arm and **11%** in the osimertinib arm

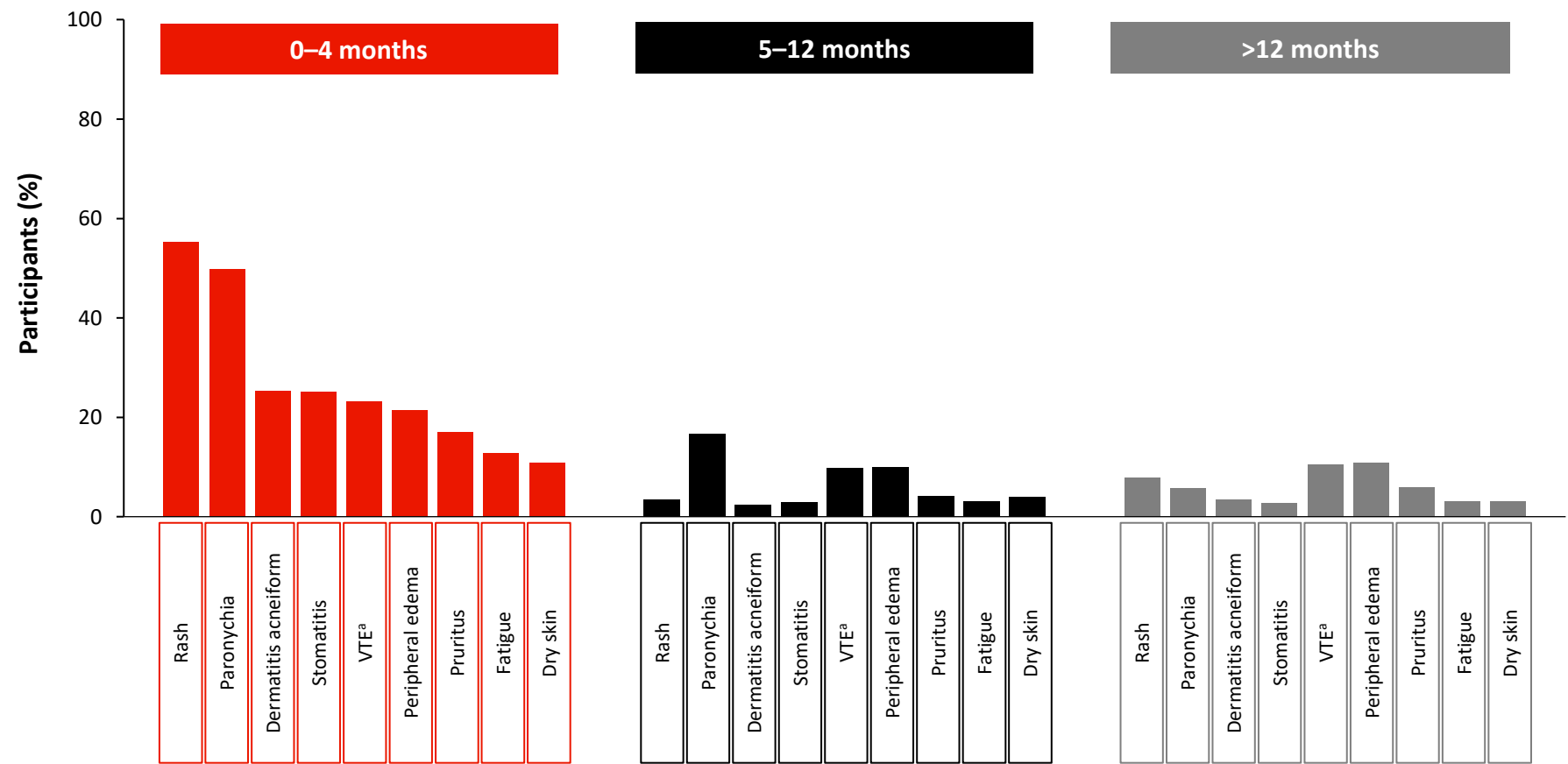
AEs by preferred term (≥20% of participants in either group)	Amivantamab + lazertinib (n=421)		Osimertinib (n=428)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Related to EGFR inhibition				
Paronychia	291 (69)	49 (12)	127 (30)	2 (<1)
Rash	271 (64)	73 (17)	136 (32)	3 (<1)
Diarrhea	133 (32)	9 (2)	200 (47)	4 (<1)
Dermatitis acneiform	127 (30)	37 (9)	55 (13)	0
Stomatitis	126 (30)	5 (1)	92 (21)	1 (<1)
Pruritus	107 (25)	2 (<1)	75 (18)	1 (<1)
Related to MET inhibition				
Hypoalbuminemia	216 (51)	26 (6)	29 (7)	0
Peripheral edema	162 (38)	8 (2)	29 (7)	1 (<1)
Other				
Infusion-related reaction	275 (65)	27 (6)	0	0
ALT increased	170 (40)	28 (7)	66 (15)	8 (2)
AST increased	139 (33)	15 (4)	68 (16)	6 (1)
Constipation	130 (31)	0	70 (16)	0
COVID-19	125 (30)	8 (2)	112 (26)	9 (2)
Anemia	114 (27)	20 (5)	112 (26)	10 (2)
Decreased appetite	114 (27)	4 (1)	84 (20)	7 (2)
Nausea	99 (24)	5 (1)	65 (15)	1 (<1)
Hypocalcemia	96 (23)	11 (3)	37 (9)	0
Asthenia	84 (20)	13 (3)	54 (13)	7 (2)
Muscle spasms	84 (20)	3 (<1)	36 (8)	0
Thrombocytopenia	74 (18)	4 (1)	92 (21)	6 (1)

^aVTE is a grouped term, which included deep vein thrombosis, limb venous thrombosis, venous thrombosis, thrombosis, superficial vein thrombosis, thrombophlebitis, embolism, venous embolism, jugular vein thrombosis, axillary vein thrombosis, post thrombotic syndrome, pelvic venous thrombosis, and superior vena cava syndrome.

1. Cho BC, et al. *N Engl J Med*. 2024;391(16):1489-1498. 2. Spira AI, et al. Presented at: 2023 North America Conference on Lung Cancer (NACLC); December 1–3, 2023; Chicago, IL, USA.

First onset of key AEs for Amivantamab + Lazertinib

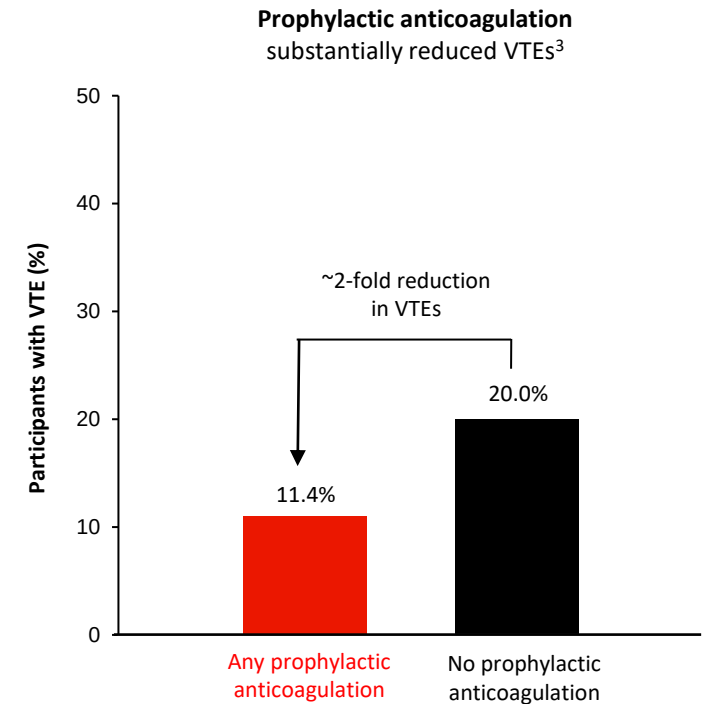
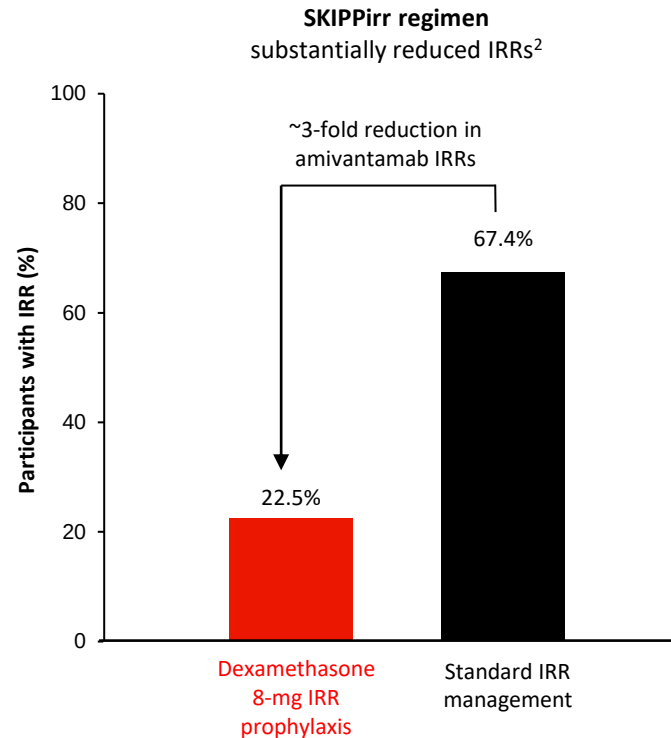
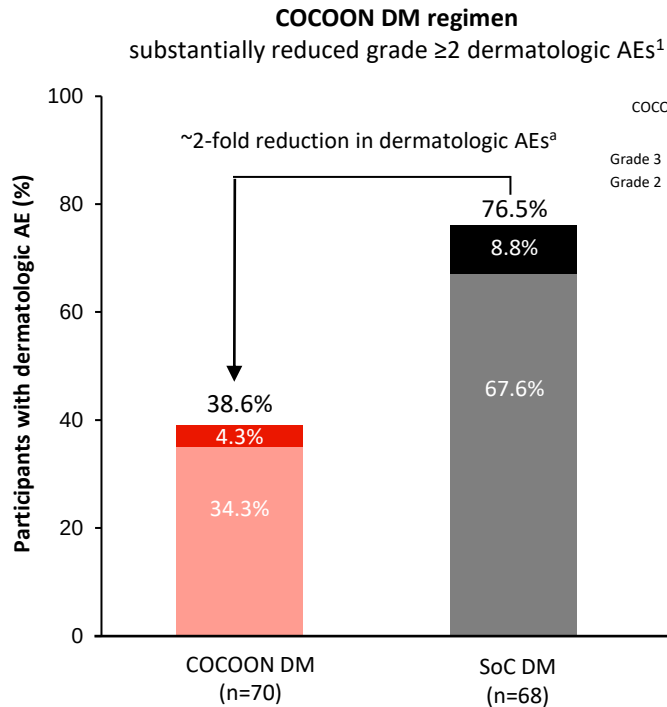
Median follow-up
of 37.8 months



Most first onset AEs occur early (0-4 months), with longer-term follow-up showing no new safety signals and indicating that long-term treatment is feasible

^aVTE is a grouped term, which included deep vein thrombosis, limb venous thrombosis, venous thrombosis, thrombosis, superficial vein thrombosis, thrombophlebitis, embolism, venous embolism, jugular vein thrombosis, axillary vein thrombosis, post thrombotic syndrome, pelvic venous thrombosis, and superior vena cava syndrome.

Early onset AEs can be significantly reduced with prophylactic approaches



Early onset AEs can be reduced using simple and accessible preventative approaches

^aOR: 0.19 (0.09–0.40); $P < 0.0001$.

1. Girard N, et al. To be presented at: The European Lung Cancer Congress (ELCC), March 26–29, 2025, Paris, France. 2. Spira AI, et al. *JTO*. 2025. In press. 3. Scott SC, et al. Presented at: American Society for Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA.

Summary

- 1L amivantamab + lazertinib led to a statistically significant reduction in mortality vs osimertinib (HR, 0.75; $P<0.005$) in participants with previously untreated *EGFR*-mutant advanced NSCLC
 - A >12-month median OS benefit is projected for amivantamab + lazertinib versus osimertinib^a
 - 60% of participants were alive at 3 years in the amivantamab + lazertinib arm vs 51% for osimertinib; benefit continued at 42-months with survival rates of 56% and 44%, respectively
- Twice as many participants receiving amivantamab + lazertinib were intracranially progression-free at 3 years (36% vs 18%) with a longer intracranial DoR vs osimertinib (35.7 vs 29.6 months)^b
- Amivantamab + lazertinib significantly delayed by a median of >14 months the time to a patient experiencing symptoms from their lung cancer (TTSP; $P<0.001$)
- AEs with amivantamab + lazertinib occurred early; prophylactic interventions have now been shown to reduce the incidence of these AEs (dermatologic AEs, IRRs and VTE)

^aBased on an exponential distribution assumption of OS in both arms, the improvement in median OS is predicted to exceed 1 year. ^bAmong participants with a history of brain metastases.

Preventing AEs with amivantamab + lazertinib



IRR Prophylactic Regimen (SKIPPirr)¹

VTE Prophylactic Regimen (PALOMA-2, PALOMA-3)^{2,3}

2 Days to 1 hour before start
Oral 8-mg dexamethasone BID
2 days and 1 day prior and
8-mg 1 hour before first infusion^a

First 4 months
Oral anticoagulants as per NCCN
or local guidelines

Dermatologic Prophylactic Regimen (COCOON)^b

**Antibiotic
prophylaxis**



Weeks 1–12
100-mg BID doxycycline
or minocycline

Weeks 13+
1% Topical clindamycin lotion
on the scalp daily

**Nail cleaning
agent**



Weeks 1+
4% Chlorhexidine on the fingernails and toenails daily for 12 months

**Long-acting
skin hydration**



Weeks 1+
Ceramide-based moisturizer at least daily for 12 months^c

^aIncludes standard premedication (antihistamines, antipyretics, and glucocorticoids). ^bProphylactic antibiotics: oral doxycycline or minocycline 100 mg BID; topical clindamycin lotion 1% on scalp daily before bedtime. Paronychia prophylaxis: chlorhexidine 4% on the fingernails and toenails daily. Skin moisturization: La Roche Posay Lipikar AP+M moisturizer on the body and face at least daily. ^cLa Roche Posay Lipikar AP+M moisturizer was used in COCOON.
AE, adverse event; BID, twice daily; IRR, infusion-related reaction; VTE, venous thromboembolism.
1. Spira AI, et al. *J Thorac Oncol*. 2025 Jan 24:S1556-0864(25)00051-6. 2. Scott SC, et al. Presented at: American Society for Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA.
3. Leighl NB, et al. *J Clin Oncol*. 2024 Oct 20;42(30):3593-3605.